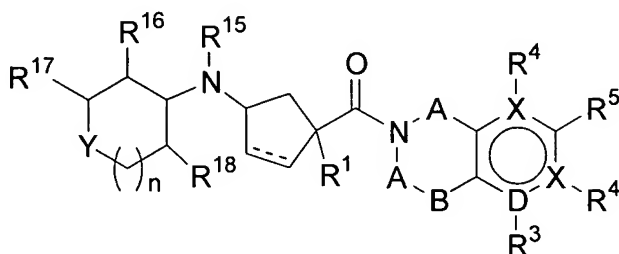


Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (currently amended) A compound of formula I:



I

wherein:

A, B, X, and D are defined as follows:

A is ~~independently selected from the group consisting of~~ CR^8R^8 , CO , NR^8 ~~and~~
 O , CR^8R^8 ,

where R^8 is independently selected from hydrogen, C_{1-6} alkyl, C_{0-4} alkyl COR^{11} and

where R^{11} is selected from the group consisting of hydroxy, hydrogen, C_{1-6} alkyl, O-
 C_{1-6} alkyl, benzyl, phenyl and C_{3-6} cycloalkyl, where said alkyl, phenyl, benzyl, and
cycloalkyl groups are unsubstituted or substituted with 1-3 substituents where said
substituents are independently selected from the group consisting of halo, hydroxy,
 C_{1-3} alkyl, C_{1-3} alkoxy, $\text{-CO}_2\text{H}$, $\text{-CO}_2\text{-C}_{1-6}$ alkyl and trifluoromethyl;

B is ~~selected from the group consisting of~~ CR^2R^2 , O , SO , SO_2 , $\text{NSO}_2\text{R}^{14}$, NCOR^{13} ,
 $\text{NCONR}^{12}\text{R}^{12}$ ~~and~~ CO , O ;

~~where R^2 is independently selected from the group consisting of hydrogen, C_{1-6} alkyl,~~
~~fluoro, hydroxy, heterocycle, NHCOR^{13} , $\text{NHSO}_2\text{R}^{14}$, and O-C_{1-6} alkyl,~~

X is carbon;

D is carbon;

where R^{12} is selected from the group consisting of hydrogen, C_{1-6} alkyl, benzyl and phenyl, and C_{3-6} cycloalkyl

where said alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents where said substituents are independently selected from the group consisting of halo, hydroxy, C_{1-3} alkyl, C_{1-3} alkoxy, $-CO_2H$, $-CO_2-C_{1-6}$ alkyl, and trifluoromethyl,

where R^{13} is selected from the group consisting of hydrogen, C_{1-6} alkyl, $-O-C_{1-6}$ alkyl, benzyl, phenyl and C_{3-6} cycloalkyl where said alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents where said substituents are independently selected from the group consisting of halo, hydroxy, C_{1-3} alkyl, C_{1-3} alkoxy, $-CO_2H$, $-CO_2-C_{1-6}$ alkyl and trifluoromethyl,

where R^{14} is selected from the group consisting of hydroxy, C_{1-6} alkyl, $-O-C_{1-6}$ alkyl, benzyl, phenyl and C_{3-6} cycloalkyl where said alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents where said substituents are independently selected from the group consisting of halo, hydroxy, C_{1-3} alkyl, C_{1-3} alkoxy, $-CO_2H$, $-CO_2-C_{1-6}$ alkyl and trifluoromethyl, and

~~where said heterocycle is unsubstituted or substituted with 1-3 substituents where said substituents are independently selected from the group consisting of halo, hydroxy, $-COR^{11}$, C_{1-3} alkyl, C_{1-3} alkoxy and trifluoromethyl;~~

~~X is carbon or nitrogen;~~

~~D is carbon, or when one of B, X and D is not CR^2R^2 , carbon, and carbon, respectively, D is a carbon or nitrogen;~~

~~provided that A, B, X, and D cannot be simultaneously CR^8R^8 , CR^2R^2 , CR^4 , and CR^3 , respectively, and that D can only be nitrogen when at least one of A, B, or X is not CR^8R^8 , CR^2R^2 , or CR^4 , respectively, where R^8 , R^2 , R^4 , and R^3 are defined below;~~

Y is selected from the group consisting of $-O-$, $-NR^{12}-$, $-S-$, $-SO-$, $-SO_2-$, and $-CR^{11}R^{11}-$, $-NSO_2R^{14}-$, $-NCOR^{13}-$, $-NCONR^{12}R^{12}-$, $-CR^{11}COR^{11}-$, $-CR^{11}OCOR^{13}-$ and $-CO-$;

R¹ is selected from the group consisting of hydrogen, -C₁₋₆alkyl, -C₀₋₆alkyl-O-C₁₋₆alkyl, -C₀₋₆alkyl-S-C₁₋₆alkyl, -(C₀₋₆alkyl)-(C₃₋₇cycloalkyl)-(C₀₋₆alkyl), hydroxy, heterocycle, -CN, -NR¹²R¹², -NR¹²COR¹³, -NR¹²SO₂R¹⁴, -COR¹¹, -CONR¹²R¹², and phenyl,

where said alkyl and said cycloalkyl are unsubstituted or substituted with 1-7 substituents where said substituents are independently selected from the group consisting of:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl,
- (d) trifluoromethyl,
- (f) C₁₋₃alkyl,
- (g) -O-C₁₋₃alkyl,
- (h) -COR¹¹,
- (i) -SO₂R¹⁴,
- (j) -NHCOCH₃,
- (k) -NHSO₂CH₃,
- (l) -heterocycle,
- (m) =O, and
- (n) -CN, and

where said phenyl and heterocycle are unsubstituted or substituted with 1-3 substituents where said substituents are independently selected from the group consisting of halo, hydroxy, -COR¹¹, C₁₋₃alkyl, C₁₋₃alkoxy and trifluoromethyl;

and where heterocycle is selected from the group consisting of benzoimidazolyl, benzofuranyl, benzofurazanyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolaziny, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthpyridinyl, oxadiazolyl, oxazolyl, oxetanyl, pyranyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxaliny, tetrahydropyranyl, tetrazolyl, tetrazolopyridyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidiny, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzoimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl,

dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolynyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidiny, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl, and N-oxides thereof;

R³ is selected from the group consisting of:

- (a) hydrogen,
- (b) C₁₋₃alkyl, optionally substituted with 1-3 fluoro,
- (c) -O-C₁₋₃alkyl, optionally substituted with 1-3 fluoro,
- (d) hydroxy,
- (e) chloro,
- (f) fluoro,
- (g) bromo,
- (h) phenyl, and
- (i) ~~heterocycle~~ and heterocycle;
- (j) ~~nothing, O, or hydrogen, when the Z bonded to R³ is nitrogen;~~

R⁴ is selected from the group consisting of:

- (a) hydrogen,
- (b) C₁₋₃alkyl, optionally substituted with 1-3 fluoro,
- (c) -O-C₁₋₃alkyl, optionally substituted with 1-3 fluoro,
- (d) hydroxy,
- (e) chloro,
- (f) fluoro,
- (g) bromo,
- (h) phenyl, and
- (i) ~~heterocycle~~ and heterocycle;
- (j) ~~nothing, O, or hydrogen, when the Z bonded to R⁴ is nitrogen;~~

R⁵ is selected from the group consisting of:

- (a) C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro and optionally substituted with hydroxyl,

- (b) -O-C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
- (c) -CO-C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
- (d) -S-C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
- (e) -pyridyl, which is unsubstituted or substituted with one or more substituents selected from the group consisting of: halo, trifluoromethyl, C₁₋₄alkyl, and COR¹¹,
- (f) fluoro,
- (g) chloro,
- (h) bromo,
- (i) -C₄₋₆cycloalkyl,
- (j) -O-C₄₋₆cycloalkyl,
- (k) phenyl, which is unsubstituted or substituted with one or more substituents selected from the group consisting of: halo, trifluoromethyl, C₁₋₄alkyl, and COR¹¹,
- (l) -O-phenyl, which is unsubstituted or substituted with one or more substituents selected from the group consisting of: halo, trifluoromethyl, C₁₋₄alkyl, and COR¹¹,
- (m) -C₃₋₆cycloalkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
- (n) -O-C₃₋₆cycloalkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
- (o) -heterocycle,
- (p) -CN and
- (q) -COR¹¹;

R¹⁵ is selected from the group consisting of:

- (a) hydrogen and
- (b) C₁₋₆alkyl, which is unsubstituted or substituted with 1-3 substituents where said substituents are independently selected from the group consisting of halo, hydroxy, -CO₂H, -CO₂C₁₋₆alkyl, and -O-C₁₋₃alkyl;

R¹⁶ is selected from the group consisting of:

- (a) hydrogen,
- (b) C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 substituents where the substituents are chosen from the group: fluoro, C₁₋₃alkoxy, hydroxy, and -COR¹¹,
- (c) fluoro,

- (d) -O-C₁₋₃alkyl, where alkyl is unsubstituted or substituted with 1-3 fluoro, ~~and~~
 - (e) C₃₋₆ cycloalkyl,
 - (f) -O-C₃₋₆cycloalkyl,
 - (g) hydroxy,
 - (h) -COR¹¹ and
 - (i) -OCOR¹³,
- or R¹⁵ and R¹⁶ may be joined together via a C₂₋₄alkyl or a C₀₋₂alkyl-O-C₁₋₃alkyl chain to form a 5-7 membered ring;

R¹⁷ is selected from the group consisting of:

- (a) hydrogen,
 - (b) C₁₋₆alkyl, where alkyl may be unsubstituted or substituted with 1-6 substituents where said substituents are chosen from the group: fluoro, C₁₋₃alkoxy, hydroxy, and -COR¹¹,
 - (c) COR¹¹,
 - (d) hydroxy, and
 - (e) -O-C₁₋₆alkyl, where alkyl may be unsubstituted or substituted with 1-6 substituents where said substituents are chosen from the ~~group~~ group consisting of fluoro, C₁₋₃alkoxy, hydroxy, and -COR¹¹,
- or R¹⁶ and R¹⁷ are joined together by a C₁₋₄alkyl chain or a C₀₋₃alkyl-O-C₀₋₃alkyl chain to form a 3-6 membered ring;

R¹⁸ is selected from the group consisting of:

- (a) hydrogen, ~~and~~
- (b) C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
- (c) fluoro,
- (d) -O-C₃₋₆cycloalkyl, and
- (e) -O-C₁₋₃alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,

or R¹⁶ and R¹⁸ are joined together by a C₂₋₃alkyl chain to form a 5-6 membered ring, where said alkyl are unsubstituted or substituted with 1-3 substituents where said substituents are independently selected from the group consisting of halo, hydroxy, -COR¹¹, C₁₋₃alkyl, and C₁₋₃alkoxy,
or R¹⁶ and R¹⁸ are joined together by a C₁₋₂alkyl-O-C₁₋₂alkyl chain to form a 6-8 membered ring, where said alkyl are unsubstituted or substituted with 1-3

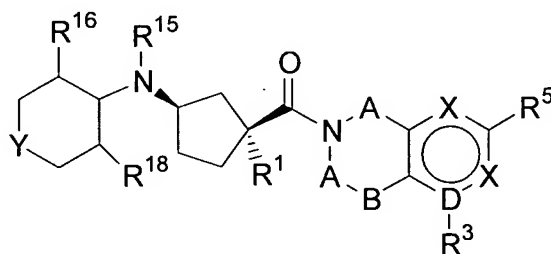
substituents where said substituents are independently selected from the group consisting of halo, hydroxy, $-\text{COR}^{11}$, C_{1-3} alkyl, and C_{1-3} alkoxy,
or R^{16} and R^{18} are joined together by a $-\text{O}-\text{C}_{1-2}\text{alkyl}-\text{O}-$ chain to form a 6-7 membered ring, where said alkyl are unsubstituted or substituted with 1-3 substituents where said substituents are independently selected from the group consisting of halo, hydroxy, $-\text{COR}^{11}$, C_{1-3} alkyl, and C_{1-3} alkoxy;

n is selected from 0, 1 and 2;

the dashed line represents a single or a double bond;

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

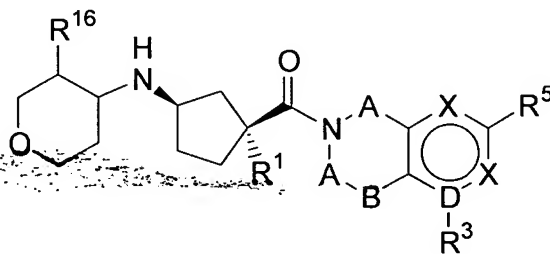
2. (original) A compound of Claim 1 of formula Ia:



Ia

wherein R^1 , R^3 , R^5 , R^{15} , R^{16} , R^{18} , A, B, D, X, and Y are defined in Claim 1, and pharmaceutically acceptable salts and individual diastereomers thereof.

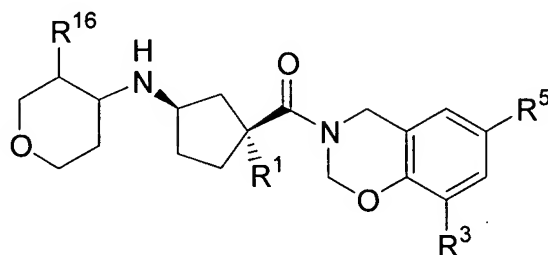
3. (original) A compound of Claim 1 of formula Ib:



Ib

wherein R^1 , R^3 , R^5 , R^{16} , A, B, D, and X are defined in Claim 1, and pharmaceutically acceptable salts and individual diastereomers thereof.

4. (original) A compound of Claim 1 of formula Ic:



Ic

wherein R^1 , R^3 , R^5 and R^{16} are defined in Claim 1, and pharmaceutically acceptable salts and individual diastereomers thereof.

Claims 5-9 (canceled)

10. (original) A compound of Claim 1 wherein Y is selected from the group consisting of: -O-, -CH₂-, -S-, -SO-, and -SO₂-.

11. (original) A compound of Claim 1 wherein R^1 is selected from the group consisting of

- (1) -C₁₋₆alkyl, which is unsubstituted or substituted with 1-6 substituents where said substituents are independently selected from the group consisting of:
 - (a) halo,
 - (b) hydroxy,
 - (c) -O-C₁₋₃alkyl,
 - (d) trifluoromethyl and
 - (e) -COR¹¹,
- (2) -C₀₋₆alkyl-O-C₁₋₆alkyl-, which is unsubstituted or substituted with 1-6 substituents where said substituents are independently selected from the group consisting of
 - (a) halo,
 - (b) trifluoromethyl and

- (c) $-\text{COR}^{\text{II}}$,
- (3) $-(\text{C}_{3-5}\text{cycloalkyl})-(\text{C}_{0-6}\text{alkyl})$, which is unsubstituted or substituted with 1-7 substituents where said substituents are independently selected from the group consisting of
 - (a) halo,
 - (b) hydroxy,
 - (c) $-\text{O}-\text{C}_{1-3}\text{alkyl}$,
 - (d) trifluoromethyl and
 - (e) $-\text{COR}^{\text{II}}$, and
- (4) phenyl or heterocycle which is unsubstituted or substituted with 1-3 substituents where said substituents are independently selected from the group consisting of
 - (a) halo,
 - (b) hydroxy,
 - (c) $-\text{O}-\text{C}_{1-3}\text{alkyl}$,
 - (d) trifluoromethyl, and
 - (e) $-\text{COR}^{\text{II}}$.

12. (original) A compound of Claim 11 wherein R^1 is $\text{C}_{1-6}\text{alkyl}$ which is unsubstituted or substituted with 1-5 substituents where said substituents are independently selected from the group consisting of:

- (a) hydroxy, and
- (b) fluoro.

13. (original) A compound of Claim 12 wherein R^1 is selected from the group consisting of:

- (a) isopropyl,
- (b) $-\text{CH}(\text{OH})\text{CH}_3$, and
- (c) $-\text{CH}_2\text{CF}_3$.

Claims 14-16 (canceled)

17. (currently amended) A compound of Claim 1 wherein ~~D is carbon and~~ R³ is selected from:

- (a) hydrogen
- (b) halo
- (c) hydroxy
- (d) C₁₋₃alkyl, where said alkyl is unsubstituted or substituted with 1-6 substituents independently selected from the group consisting of fluoro, and hydroxy,
- (e) -COR¹¹,
- (f) -CONR¹²R¹²,
- (g) -heterocycle,
- (h) -NR¹²-SO₂-NR¹²R¹²,
- (i) -NR¹²-SO₂-R¹⁴,
- (j) -SO₂-NR¹²R¹²,
- (k) -nitro and
- (l) -NR¹²R¹².

18. (currently amended) A compound of Claim 17 ~~16~~ wherein ~~D is carbon and~~ R³ is selected from the group consisting of:

- (a) fluoro,
- (b) trifluoromethyl and
- (c) hydrogen.

19. (currently amended) A compound of Claim 18 wherein ~~D is carbon and~~ R³ is

- (a) fluoro or
- (b) hydrogen.

20-21 (canceled)

22. (currently amended) A compound of Claim 1 ~~20~~ wherein ~~X is carbon and~~ R⁴ is selected from the group consisting of:

- (a) hydrogen,
- (b) trifluoromethyl and

(c) halo.

23. (currently amended) A compound of Claim 22 wherein ~~X is carbon~~ and R⁴ is hydrogen.

24. (original) A compound of Claim 1 wherein R⁵ is selected from the group consisting of

- (a) C₁₋₃alkyl substituted with 1-6 fluoro,
- (b) chloro,
- (c) bromo,
- (d) -O-phenyl, which is unsubstituted or substituted with one or more substituents selected from the group consisting of: halo and trifluoromethyl,
- (e) phenyl, which is unsubstituted or substituted with one or more substituents selected from the group consisting of: halo and trifluoromethyl, and
- (f) -O-C₁₋₃alkyl substituted with 1-6 fluoro.

25. (original) A compound of Claim 24 wherein R⁵ is selected from the group consisting of:

- (a) trifluoromethyl,
- (b) trifluoromethoxy,
- (c) bromo, and
- (d) chloro.

26. (original) A compound of Claim 25 wherein R⁵ is selected from trifluoromethyl and trifluoromethoxy.

27. (original) A compound of Claim 1 wherein R¹⁵ is hydrogen or methyl.

28. (original) A compound of Claim 1 wherein R¹⁶ is selected from the group consisting of:

- (a) hydrogen,
- (b) C₁₋₃alkyl, which is unsubstituted or substituted with 1-6 fluoro,
- (c) -O-C₁₋₃alkyl,
- (d) fluoro, and
- (e) hydroxy.

29. (original) A compound of Claim 28 wherein R^{16} is selected from the group consisting of:

- (a) hydrogen,
- (b) trifluoromethyl,
- (c) methyl,
- (d) methoxy,
- (e) ethoxy,
- (f) ethyl,
- (g) fluoro, and
- (h) hydroxy.

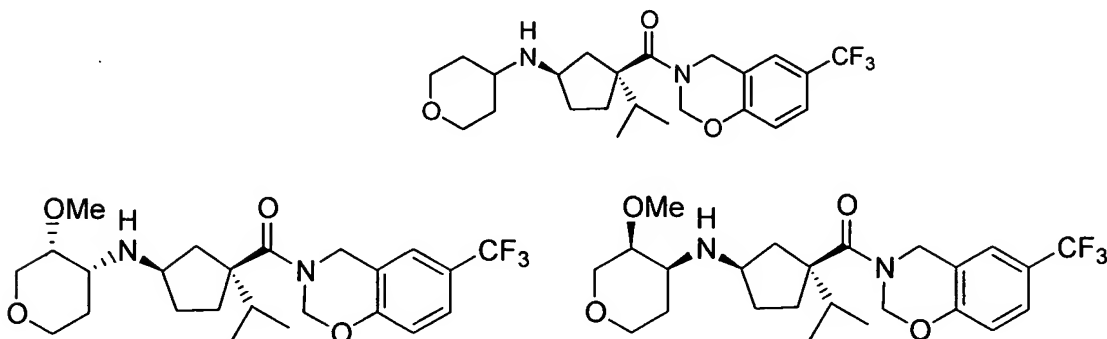
30. (original) A compound of Claim 29 wherein R^{16} is selected from the group consisting of:

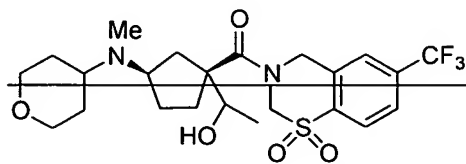
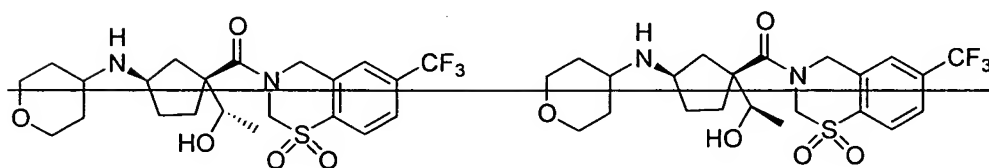
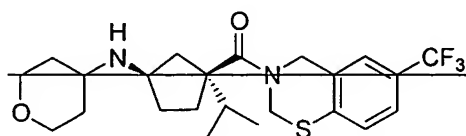
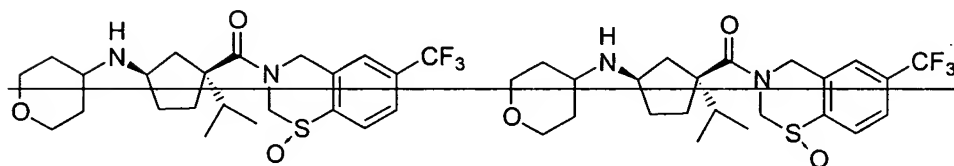
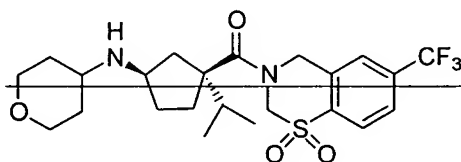
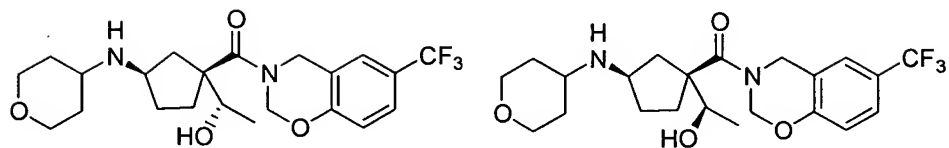
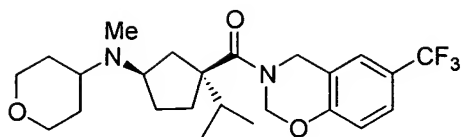
- (a) hydrogen,
- (b) methyl, and
- (c) methoxy.

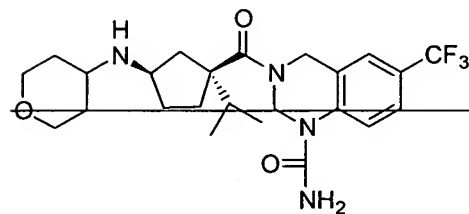
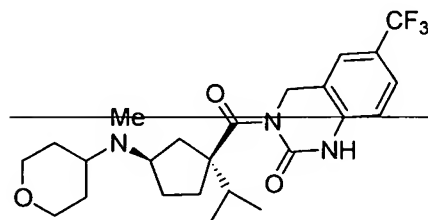
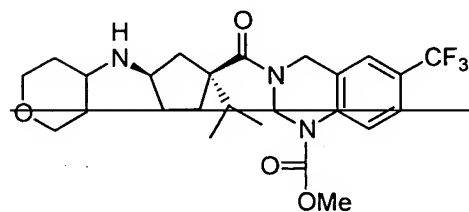
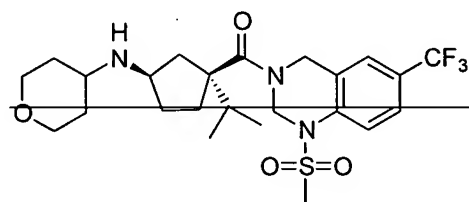
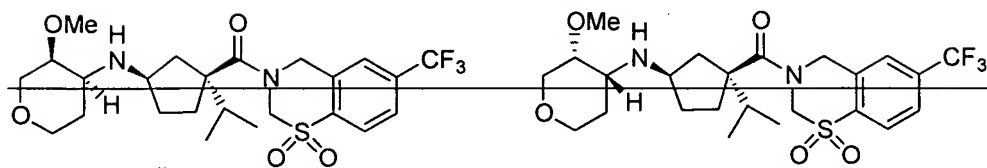
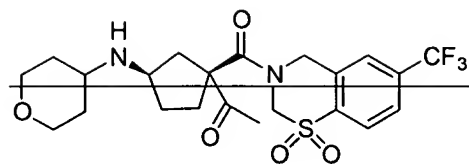
31. (original) A compound of Claim 1 wherein R^{18} is selected from the group consisting of:

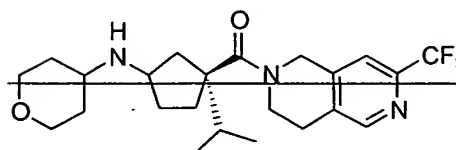
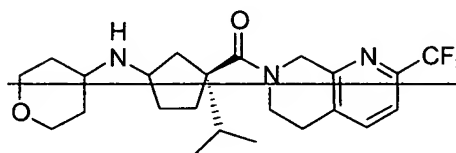
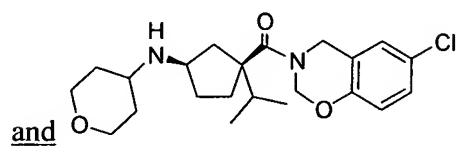
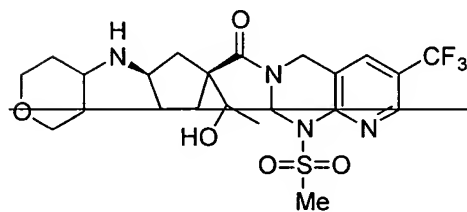
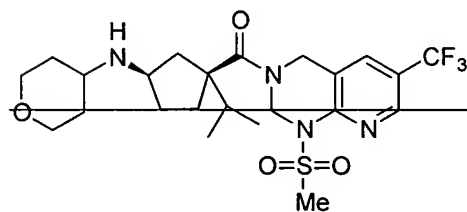
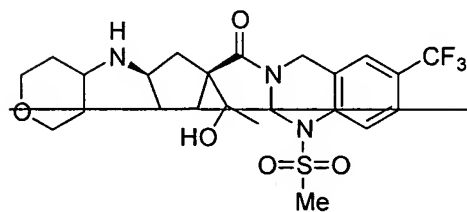
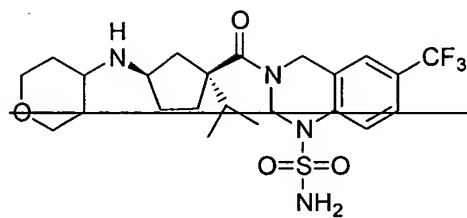
- (a) hydrogen,
- (b) methyl, and
- (c) methoxy.

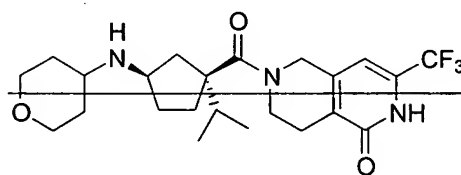
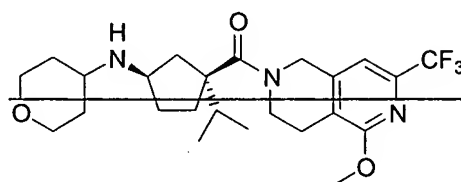
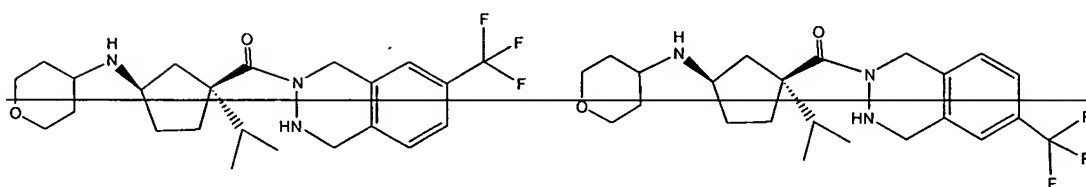
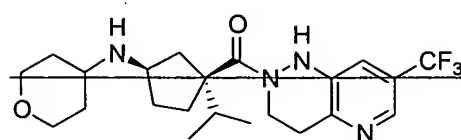
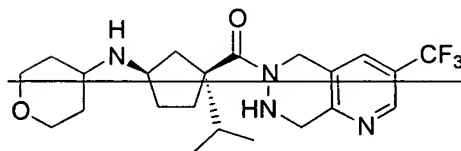
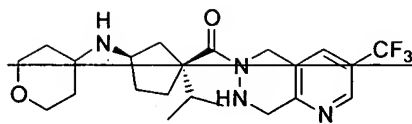
32. (currently amended) One or more compounds of Claim 1 selected from the group consisting of:



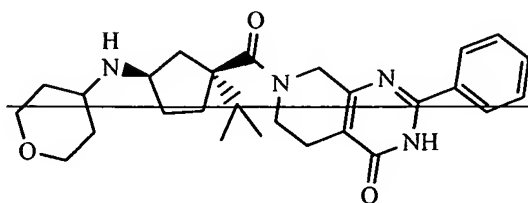








and



33. (original) A compound of Claim 1 wherein R¹⁶ and R¹⁸ are joined together by a -CH₂CH₂- chain or a -CH₂CH₂CH₂- chain to form a cyclopentyl ring or a cyclohexyl ring.

34. (original) A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.

35. (currently amended) A method for modulation of chemokine receptor CCR-2 activity ~~in a mammal~~ in vitro which comprises the administration of an effective amount of the compound of Claim 1.

36. (currently amended) A method for ~~treating, ameliorating, controlling or reducing the risk of an inflammatory and immunoregulatory disorder or disease~~ treating atherosclerosis which comprises the administration to a patient of an effective amount of the compound of Claim 1.

37. (original) A method for treating, ameliorating, controlling or reducing the risk of rheumatoid arthritis which comprises the administration to a patient of an effective amount of the compound of Claim 1.